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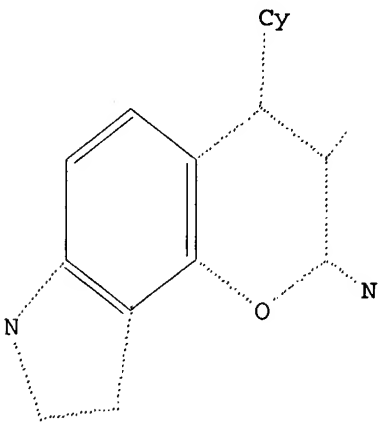
L2 STRUCTURE UPLOADED

=> d l2
L2 HAS NO ANSWERS
L2 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 1919 TO ITERATE

100.0% PROCESSED 1919 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 35753 TO 41007
PROJECTED ANSWERS: 3 TO 163

L3 3 SEA SSS SAM L2

=> s l2 full
FULL SEARCH INITIATED 16:25:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 38300 TO ITERATE

100.0% PROCESSED 38300 ITERATIONS 88 ANSWERS
SEARCH TIME: 00.00.01

L4 88 SEA SSS FUL L2

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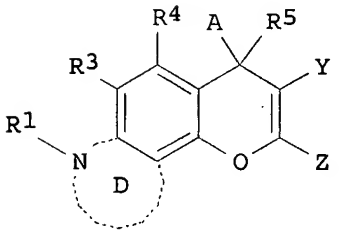
ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
2003:931479 Document No. 140:5049 Preparation of substituted 4-aryl-4H-pyrrolo[2,3-h]chromenes and analogs as activators of caspases and inducers of apoptosis and their uses against cancer and other disorders. Cai, Sui Xiong; Jiang, Songchun; Kemnitzer, William E.; Zhang, Hong; Attardo, Giorgio; Denis, Real (Cytovia, Inc., USA; Shire Biochem, Inc.). PCT Int. Appl. WO 2003097806 A2 20031127, 110 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US15427 20030516. PRIORITY: US 2002-378079P 20020516.

GI



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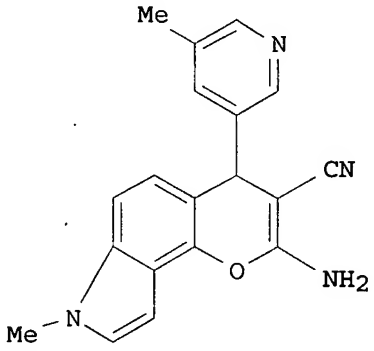


II

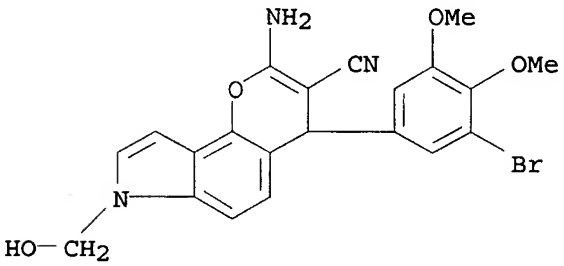
AB The present invention is directed to substituted 4-aryl-4H-pyrrolo[2,3-h]chromenes and analogs thereof (shown as I; variables defined below; e.g. II). The present invention also relates to the discovery that compds. I are activators of caspases and inducers of apoptosis. Therefore, I can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. The ability to activate the caspase cascade and induce apoptosis in human breast cancer cell lines T-47D and ZR-75-1 was measured for .apprx.50 examples of I, e.g. EC50 (nM) = 2.3 and 1.6, resp., for II. Although the methods of preparation are not claimed, .apprx.50 example prepns. are included. For I: R1 = alkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, haloalkyl, alkoxyalkyl, aminoalkyl and oxiranylalkyl; R3 and R4 = H, halo, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, C1-10 alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthio; R5 is H or C1-10 alkyl. A is (un)substituted and is aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl; D is (un)substituted and is a heteroarom., partially saturated (un)saturated heterocyclic fused ring, wherein said fused ring has 5 or 6 ring atoms, wherein one or two of said ring atoms are N atoms and the others of said ring atoms are C atoms. Y is CN, COR19, CO2R19 or CONR20R21, wherein R19, R20 and R21 = H, C1-10-alkyl, haloalkyl, aryl, fused aryl,

carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or R20 and R21 are taken together with the N to form a heterocycle; and Z is NR22R23, NHCOR22N(COR23)2, N(COR22)(COR23), N:CHOR19 or N:CHR19 wherein R22 and R23 = H, C1-4 alkyl or aryl, or R22 and R23 are combined together with the group attached to them to form a heterocycle.

IT **627501-36-4P**, 2-Amino-4-(3-bromo-4,5-dimethoxyphenyl)-3-cyano-7-hydroxymethyl-4H-pyrrolo[2,3-h]chromene **627501-48-8P**, 2-Amino-3-cyano-4-(5-methylpyridin-3-yl)-7-hydroxymethyl-4H-pyrrolo[2,3-h]chromene
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of substituted 4-aryl-4H-pyrrolo[2,3-h]chromenes and analogs as activators of caspases and inducers of apoptosis and their uses against cancer and other disorders)

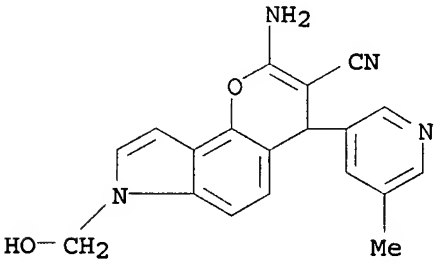
RN 627501-36-4 CAPLUS

CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4-(3-bromo-4,5-dimethoxyphenyl)-4,7-dihydro-7-(hydroxymethyl)- (9CI) (CA INDEX NAME)



RN 627501-48-8 CAPLUS

CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4,7-dihydro-7-(hydroxymethyl)-4-(5-methyl-3-pyridinyl)- (9CI) (CA INDEX NAME)



IT **475577-56-1P**, 2-Amino-4-(3-bromo-4,5-dimethoxyphen

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ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

2003:931119 Document No. 140:5041 Preparation of substituted 4H-chromenes, 2H-chromenes, chromans and analogs as activators of caspases and inducers of apoptosis and their uses against cancer and other disorders. Cai, Sui Xiong; Jiang, Songchun; Attardo, Giorgio; Denis, Real; Storer, Richard; Rej, Rabindra (Cytovia, Inc., USA; Shire Biochem, Inc.). PCT Int. Appl. WO 2003096982 A2 20031127, 116 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US15432 20030516. PRIORITY: US 2002-378043P 20020516.

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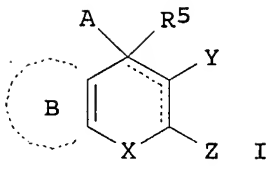
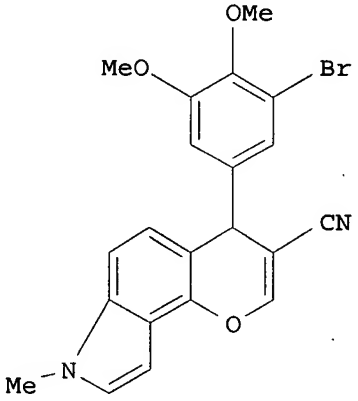


I



II

AB The present invention is directed to substituted 4H-chromenes, 2H-chromenes, chromans and analogs thereof (shown as I; variables defined below; e.g. II). The present invention also relates to the discovery that compds. I are activators of caspases and inducers of apoptosis. Therefore, I can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. The ability to activate the caspase cascade and induce apoptosis in human breast cancer cell lines T-47D and ZR-75-1 was measured for .apprx.30 examples of I, e.g. EC50 (nM) = 2.7 and 2.2, resp., for II. Although the methods of preparation are not claimed, .apprx.30 example prepns. are included. For I: X is O, S or NR6, wherein R6 is H or (un)substituted alkyl; Y is H, halogen, CN, COR7, CO2R7 or CONRxRy, wherein R7, Rx and Ry = H, C1-10-alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or Rx and Ry are taken together with the N to which they are attached to form a heterocycle. Z is H, OH, OR8, OCOR8, wherein R8 is H, C1-10 alkyl, haloalkyl, aryl, fused aryl, carbocyclic, a heterocyclic group, a heteroaryl group, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl, when the dotted line between C atoms bonded to groups Y and Z is not present Z can be dialkyl. R5 is H or C1-10-alkyl; A is (un)substituted and is aryl, heteroaryl, saturated

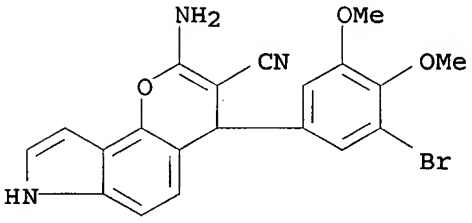
carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic, arylalkyl or heteroarylalkyl; B is an (un)substituted aromatic or heteroarom. ring; and the dotted lines are single or double bonds, provided that both sets of dotted lines cannot be double bonds at the same time and R5 is not present when the dotted line between C atoms bonded to groups A and Y is a double bond.

IT **339062-49-6 627501-23-9**

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted chromenes, chromans and analogs as activators of caspases and inducers of apoptosis and their uses against cancer and other disorders)

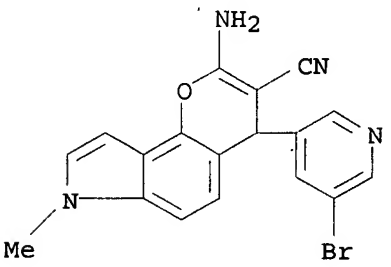
RN 339062-49-6 CAPLUS

CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4-(3-bromo-4,5-dimethoxyphenyl)-4,7-dihydro- (9CI) (CA INDEX NAME)



RN 627501-23-9 CAPLUS

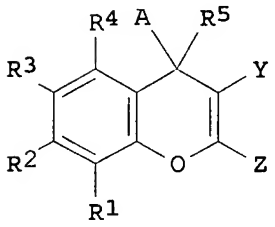
CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4-(5-bromo-3-pyridinyl)-4,7-dihydro-7-methyl- (9CI) (CA INDEX NAME)



ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

2002:888735 Document No. 137:369971 Preparation of substituted 4H-chromenes and analogs as activators of caspases and inducers of apoptosis and their uses against cancer and other disorders. Cai, Sui Xiong; Zhang, Hong; Jiang, Songchun; Storer, Richard (Cytovia, Inc., USA). PCT Int. Appl. WO 2002092594 A1 20021121, 139 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US15399 20020516. PRIORITY: US 2001-290997P 20010516.

GI



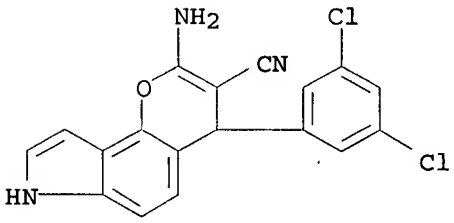
I

AB The present invention is directed to substituted 4H-chromenes and analogs thereof (shown as I; e.g. 2-amino-3-cyano-7-hydroxy-4-(3-bromo-4,5-dimethoxyphenyl)-4H-chromene). It also relates to the discovery that I are activators of caspases and inducers of apoptosis and, therefore, can be used to induce cell death in a variety of clin. conditions in which controlled growth and spread of abnormal cells occurs. In I: R1-R4 = H, halo, haloalkyl, aryl, fused aryl, carbocyclic, heterocyclic, heteroaryl, C1-10 alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, nitro, amino, cyano, acylamido, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, methylenedioxy, carbonylamido or alkylthio; or R1 and R2, or R2 and R3, or R3 and R4, taken together with the atoms to which they are attached form an aryl, heteroaryl, partially saturated carbocyclic or partially saturated heterocyclic group, wherein said group is optionally substituted. R5 is H or C1-10 alkyl; A is optionally substituted and is aryl, heteroaryl, saturated carbocyclic, partially saturated carbocyclic, saturated heterocyclic, partially saturated heterocyclic or arylalkyl; Y is CN, COR7, CO2R7 or CONRxRy, wherein R7, Rx and Ry = H, C1-10 alkyl, haloalkyl, aryl, fused aryl, carbocyclic, heterocyclic, heteroaryl, alkenyl, alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl or aminoalkyl; or Rx and Ry are taken together with the N to which they are attached to form a heterocycle; and Z is NR8R9, NHCOR8, N(COR9)2, N(COR8)(COR9), N:CHOR8 or N:CHR8, wherein R8 and R9 = H, C1-4 alkyl or aryl, or R8 and R9 are combined together with the group attached to them to form a heterocycle. The EC50 values for >80 I against T-47D and ZR-75-1 human breast cancer cell lines are tabulated, e.g. 30 and 25 nM, resp., for 2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[7,6-b]pyran. Although the methods of preparation are not claimed, 81 example prepns. are included.

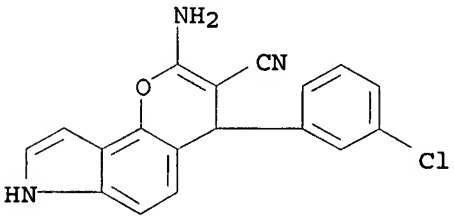
IT **475576-49-9P**, 2-Amino-3-cyano-4-(3,5-dichlorophenyl)-4H-indolo[4,5-b]pyran **475576-50-2P**, 2-Amino-3-cyano-4-(3-chlorophenyl)-4H-

indolo[4,5-b]pyran **475576-54-6P**, 2-Amino-3-cyano-4-(3,5-difluorophenyl)-4H-indolo[4,5-b]pyran **475576-55-7P**, 2-Amino-3-cyano-4-(3-fluorophenyl)-4H-indolo[4,5-b]pyran **475576-66-0P**, 2-Amino-3-cyano-4-(3-pyridyl)-4H-indolo[4,5-b]pyran **475576-75-1P**, 2-Amino-3-cyano-4-(5-methyl-3-pyridyl)-4H-indolo[4,5-b]pyran **475576-76-2P**, 2-Amino-3-cyano-4-(5-bromo-3-pyridyl)-4H-indolo[4,5-b]pyran **475576-79-5P**, 2-Amino-3-cyano-4-(5-methoxypyridin-3-yl)-4H-indolo[4,5-b]pyran **475576-84-2P**, 2-Amino-3-cyano-4-(3-methoxyphenyl)-4H-indolo[4,5-b]pyran **475576-89-7P**, 2-Amino-4-(3-bromo-4-hydroxy-5-methoxyphenyl)-3-cyano-4H-indolo[4,5-b]pyran **475576-95-5P**, 2-Amino-3-cyano-4-phenyl-4H-indolo[4,5-b]pyran **475576-96-6P**, 2-Amino-3-cyano-4-(5-cyano-pyridin-3-yl)-4H-indolo[4,5-b]pyran **475576-97-7P**, 2-Amino-3-cyano-4-(6-methylpyrazin-2-yl)-4H-indolo[4,5-b]pyran **475576-98-8P**, 2-Amino-3-cyano-4-(quinoxalin-2-yl)-4H-indolo[4,5-b]pyran **475577-15-2P**, 2-Amino-3-cyano-4-(3-bromo-4-phosphoric acid dipiperidine salt-5-methoxyphenyl)-4H-indolo[4,5-b]pyran **475577-26-5P**, 2-Amino-3-ethoxycarbonyl-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran **475577-27-6P**, 2-Amino-3-methoxycarbonyl-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran **475577-56-1P**, 2-Amino-4-(3-bromo-4,5-dimethoxyphenyl)-3-cyano-7-ethyl-4H-pyrrolo[2,3-h]chromene **475577-57-2P**, 2-Amino-4-(3-bromo-4,5-dimethoxyphenyl)-3-cyano-7-cyclopropylmethyl-4H-pyrrolo[2,3-h]chromene **475577-58-3P**, 2-Amino-4-(3-bromo-4,5-dimethoxyphenyl)-3-cyano-7-(2-diethylaminoethyl)-4H-pyrrolo[2,3-h]chromene
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of substituted 4H-chromenes and analogs as activators of caspases and inducers of apoptosis and their uses against cancer and other disorders)

RN 475576-49-9 CAPLUS
CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4-(3,5-dichlorophenyl)-4,7-dihydro- (9CI) (CA INDEX NAME)



RN 475576-50-2 CAPLUS
CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4-(3-chlorophenyl)-4,7-dihydro- (9CI) (CA INDEX NAME)



RN 475576-54-6 CAPLUS

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CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4-(3,5-difluorophenyl)-4,7-dihydro- (9CI) (CA INDEX NAME)

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

2002:888548 Document No. 137:384750 Preparation of substituted coumarins and quinolinones as caspase activators for treatment of cancer. Cai, Sui Xiong; Zhang, Hong; Kemmitzer, William E.; Jiang, Songchun; Drewe, John A.; Storer, Richard (Cytovia, Inc., USA; Shire Biochem, Inc.). PCT Int. Appl. WO 2002092076 A1 20021121, 84 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US15401 20020516. PRIORITY: US 2001-290978P 20010516.

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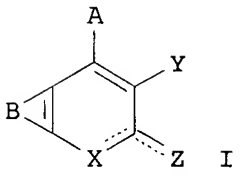

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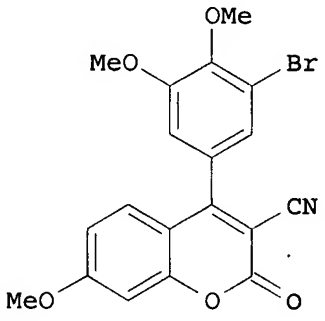


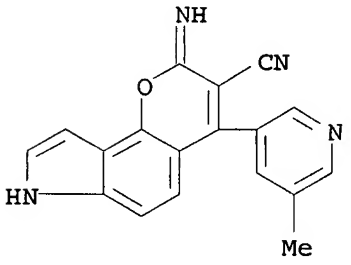
II

AB Title compds. I [wherein X = O, S or NR6; R6 = H or (un)substituted alkyl or aryl; Y = CN, COR7, CO2R7, or CONR9R10; R7, R9, and R10 = independently H, (halo)alkyl, (fused) aryl, carbocyclyl, heterocyclyl, heteroaryl, alkenyl, alkynyl, (hetero)arylalkyl, (hetero)arylalkenyl, (hetero)arylalkynyl, (hetero)cycloalkyl, hydroxyalkyl, or aminoalkyl; or NR9R10 = heterocyclyl; Z = O, S, halo, NR8, or NCOR8; R8 = independently H, alkyl, or aryl; A = (un)substituted (hetero)aryl, (hetero)cyclyl, or (hetero)arylalkyl; B = (un)substituted (hetero)aryl or (hetero)cyclyl; or pharmaceutically acceptable salts or prodrugs thereof] were prepared as caspase activators and inducers of apoptosis. For example, condensation of 5-bromoveratraldehyde with Et cyanoacetate in EtOH in the presence of piperidine gave 3-(3-bromo-4,5-dimethoxyphenyl)-2-cyanoacrylic acid Et ester. Treatment of the acrylate with a solution of 3-methoxyphenol and NaH in toluene afforded the coumarin II (1.7%). The latter induced apoptosis in the human breast cancer cell lines T-47D and ZR-75-1 with EC50 values of 257 nM and 97 nM, resp. Therefore, I, optionally administered with at least one known cancer chemotherapeutic agent, are useful for the treatment of cancer.

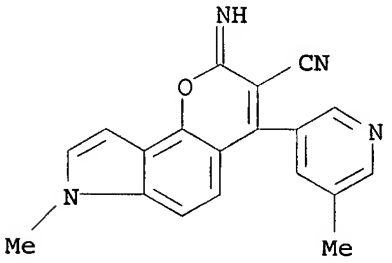
IT **475629-54-0P**, 3-Cyano-2-imino-4-(5-methylpyridin-3-yl)-2H-pyrrolo[2,3-h]chromene **475629-60-8P**, 3-Cyano-2-imino-7-methyl-4-(5-methylpyridin-3-yl)-2H-pyrrolo[2,3-h]chromene **475629-66-4P**, 4-(3-Bromo-4,5-dimethoxyphenyl)-3-cyano-2-imino-7-methyl-2H-pyrrolo[2,3-h]chromene **475630-01-4P**, 3-Cyano-2-imino-7-methyl-4-(3-nitrophenyl)-2H-pyrrolo[2,3-h]chromene **475630-03-6P**, 3-Cyano-2-imino-7-methyl-4-(3,4,5-trimethoxyphenyl)-2H-pyrrolo[2,3-h]chromene **475630-05-8P**, 3-Cyano-4-(3,5-dimethoxyphenyl)-2-imino-7-methyl-2H-pyrrolo[2,3-h]chromene **475630-07-0P**,

3-Cyano-2-imino-4-(3-methoxy-4,5-methylenedioxyphenyl)-7-methyl-2H-pyrrolo[2,3-h]chromene **475630-09-2P**, 3-Cyano-2-imino-4-(3-methoxyphenyl)-7-methyl-2H-pyrrolo[2,3-h]chromene **475630-11-6P**, 3-Cyano-2-imino-4-(3-bromophenyl)-7-methyl-2H-pyrrolo[2,3-h]chromene
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(anticancer agent; preparation of substituted coumarin and quinolinone anticancer agents from aldehydes, ketones, cyanoacetates, and phenols)

RN 475629-54-0 CAPLUS
CN Pyrano[2,3-e]indole-3-carbonitrile, 2,7-dihydro-2-imino-4-(5-methyl-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 475629-60-8 CAPLUS
CN Pyrano[2,3-e]indole-3-carbonitrile, 2,7-dihydro-2-imino-7-methyl-4-(5-methyl-3-pyridinyl)- (9CI) (CA INDEX NAME)

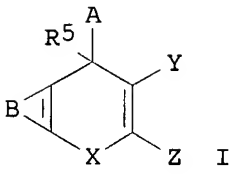


RN 475629-66-4 CAPLUS
CN Pyrano[2,3-e]indole-3-carbonitrile, 4-(3-bromo-4,5-dimethoxyphenyl)-2,7-dihydro-2-imino-7-methyl- (9CI) (CA INDEX NAME)

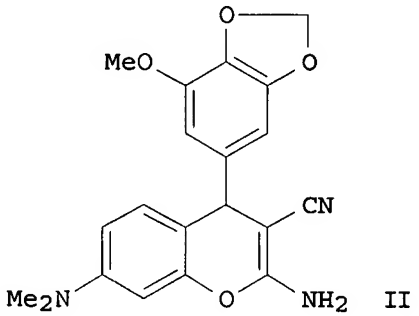
ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

2001:359984 Document No. 134:353254 Substituted 4H-chromene and analogs as activators of caspases and inducers of apoptosis and the use thereof. Drewe, John A.; Cai, Sui Xiong; Wang, Yan (Cytovia, Inc., USA). PCT Int. Appl. WO 2001034591 A2 20010517, 148 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US30374 20001103. PRIORITY: US 1999-PV163584 19991105; US 2000-PV185211 20000224.

GI



I



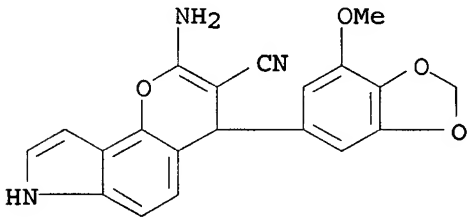
II

AB Title compds. (I) [wherein X = O or S; Y = CN, COR7, CO2R7, or CONRxRy; R7, Rx, and Ry = independently H, (halo)alkyl, (hetero)aryl, fused aryl, carbocyclic, heterocyclic, alkenyl, alkynyl, (hetero)arylalkyl, (hetero)arylalkenyl, (hetero)arylalkynyl, carbocycloalkyl, heterocycloalkyl, hydroxyalkyl, or aminoalkyl; or Rx and Ry taken together with the N to which they are attached form a heterocycle; Z = NR8R9, NHCOR8, N(COR8)2, N(COR8)(COR9), N:CHOR8, or N:CHR8; R8 and R9 = independently H, alkyl, or aryl; or R8 and R9 taken together with the group to which they are attached form a heterocycle; R5 = H or alkyl; A = (un)substituted (hetero)aryl, carbocyclic, heterocyclic, or arylalkyl; B = (un)substituted (hetero)aromatic ring] were prepared as activators of caspases and inducers of apoptosis. For example, piperidine was added to a mixture of 3-dimethylaminophenol, 5-methoxypiperonal, and malonitrile in EtOH to give II (74%). In assays against the human breast cancer cell lines T-47D and ZR-75-1, II showed potent caspase activity (determined as the ratios of net relative fluorescence units for test compds. compared to control samples of 5.5 and 6.3, resp.) and potency (EC50 = 87 nM and 38 nM, resp.). II also inhibited cell proliferation with GI50 values of 3 nM and 500 nM against T-47D and ZR-75-1, resp. Thus, I may be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs.

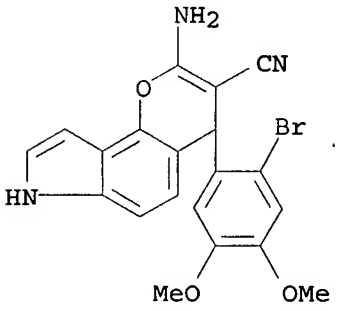
IT **339062-46-3P**, 2-Amino-3-cyano-4-(3-methoxy-4,5-methylenedioxyphenyl)-4H-indolo[4,5-b]pyran **339062-47-4P**, 2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran **339062-48-5P**, 2-Amino-3-cyano-4-(2-bromo-4,5-dimethoxyphenyl)-8-methyl-4H-indolo[4,5-b]pyran **339062-49-6P**, 2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran **339062-50-9P**, 2-Amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-8-methyl-4H-indolo[4,5-b]pyran **339062-51-0P**, 2-Amino-3-cyano-4-(3,4,5-trimethoxyphenyl)-4H-indolo[4,5-b]pyran **339062-52-1P**, 2-Amino-3-cyano-4-(3-nitrophenyl)-4H-indolo[4,5-b]pyran **339062-53-2P**,

2-Amino-3-cyano-4-(3,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran **339062-54-3P**, 2-Amino-3-cyano-4-(3-cyanophenyl)-4H-indolo[4,5-b]pyran **339062-88-3P**, 9-Acetamido-2-amino-3-cyano-4-(3-bromo-4,5-dimethoxyphenyl)-4H-indolo[4,5-b]pyran
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 4H-chromene and analogs as activators of caspases and inducers of apoptosis)

RN 339062-46-3 CAPLUS
CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4,7-dihydro-4-(7-methoxy-1,3-benzodioxol-5-yl)- (9CI) (CA INDEX NAME)



RN 339062-47-4 CAPLUS
CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4-(2-bromo-4,5-dimethoxyphenyl)-4,7-dihydro- (9CI) (CA INDEX NAME)



RN 339062-48-5 CAPLUS
CN Pyrano[2,3-e]indole-3-carbonitrile, 2-amino-4-(2-bromo-4,5-dimethoxyphenyl)-4,7-dihydro-8-methyl- (9CI) (CA INDEX NAME)

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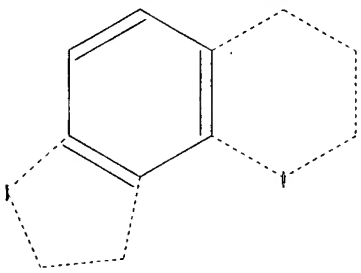

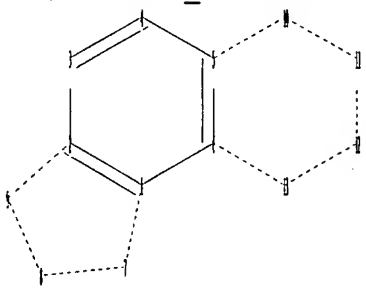

ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13
ring bonds :
1-2 1-6 1-7 2-3 2-9 3-4 4-5 5-6 5-10 6-13 7-8 8-9 10-11 11-12 12-13

exact/norm bonds :
1-7 2-9 5-10 6-13 7-8 8-9 10-11 11-12 12-13
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom

L6 STRUCTURE UPLOADED

=> s l6 full
FULL SEARCH INITIATED 16:42:13 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 157007 TO ITERATE

100.0% PROCESSED 157007 ITERATIONS 274 ANSWERS
SEARCH TIME: 00.00.01

L7 274 SEA SSS FUL L6

10514427

(FILE 'HOME' ENTERED AT 16:22:23 ON 02 MAY 2007)

FILE 'REGISTRY' ENTERED AT 16:22:34 ON 02 MAY 2007
L1 STRUCTURE UPLOADED

FILE 'STNGUIDE' ENTERED AT 16:23:25 ON 02 MAY 2007

FILE 'REGISTRY' ENTERED AT 16:25:19 ON 02 MAY 2007
L2 STRUCTURE UPLOADED
L3 3 S L2
L4 88 S L2 FULL

FILE 'CAPLUS' ENTERED AT 16:26:28 ON 02 MAY 2007
L5 5 S L4

FILE 'STNGUIDE' ENTERED AT 16:27:16 ON 02 MAY 2007

FILE 'REGISTRY' ENTERED AT 16:41:58 ON 02 MAY 2007
L6 STRUCTURE UPLOADED
L7 274 S L6 FULL

FILE 'CAPLUS' ENTERED AT 16:42:31 ON 02 MAY 2007
L8 55 S L7

FILE 'STNGUIDE' ENTERED AT 16:43:34 ON 02 MAY 2007

FILE 'REGISTRY' ENTERED AT 16:46:57 ON 02 MAY 2007
L9 1 S 849100-59-0/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY

FILE 'STNGUIDE' ENTERED AT 16:47:21 ON 02 MAY 2007

FILE 'REGISTRY' ENTERED AT 16:49:22 ON 02 MAY 2007
L10 1 S 113707-93-0/RN
SET NOTICE 1 DISPLAY
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FILE 'STNGUIDE' ENTERED AT 16:49:38 ON 02 MAY 2007

FILE 'REGISTRY' ENTERED AT 16:52:13 ON 02 MAY 2007

FILE 'STNGUIDE' ENTERED AT 16:54:34 ON 02 MAY 2007

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IC ICM C07D471-06
ICS C07D471-16; C07D487-06; C07D491-16; C07D495-16; C07D498-06; C07D513-06; A61K031-495; A61K031-535; A61K031-54

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

TI Preparation of fused polycyclic heterocycle derivatives such as benzo[c]pyrimido[5,6,1-jk]carbazole-4,6(5H)-dione derivatives as antitumor agents

ST fused polycyclic heterocycle prepn antitumor; benzopyrimidocarbazoledione prepn antitumor

IT Antitumor agents
(preparation of fused polycyclic heterocycle derivs. such as benzopyrimidocarbazoledione derivs. as antitumor agents)

IT 924-44-7, Ethyl glyoxylate
RL: RCT (Reactant); RACT (Reactant or reagent)
(polymer-type; preparation of fused polycyclic heterocycle derivs. such as benzopyrimidocarbazoledione derivs. as antitumor agents)

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55 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
CC 8-9 (Radiation Biochemistry)
TI Synthesis and antiproliferative activity of furocoumarin isosteres
ST furocoumarin isostere prepn phototherapy skin disease
IT Photosensitizers
Psoriasis
Skin, disease
(furocoumarin isosteres synthesis and skin antiproliferative activity)
IT Furocoumarins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(furocoumarin isosteres synthesis and skin antiproliferative activity)
IT Phototherapy
(chemo-, furocoumarin isosteres synthesis a

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55 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
IC ICM C07D491-06
ICS A61K031-40
CC 27-14 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
TI Preparation of 2-aminomethyl-3,4,7,9-tetrahydro-2H-pyrano[2,3-e]indol-8-ones as dopamine autoreceptor agonists
ST aminomethylpyranoindolone prepn dopamine autoreceptor agonist; D2 dopaminergic agonist aminomethylpyranoindolone prepn; schizophrenia aminomethylpyranoindolone prepn; Parkinson's disease aminomethylpyranoindolone prepn; hyperprolactinemia aminomethylpyranoindolone prepn; antidepressant aminomethylpyranoindolone prepn; Tourette's syndrome aminomethylpyranoindolone prepn; drug dependence aminomethylpyranoindolone prepn; alcoholism aminomethylpyranoindolone prepn

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55 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
CC 26-4 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 10
TI Synthesis of 4-hydroxy-1-methylindole and benzo[b]thiophen-4-ol based unnatural flavonoids as new class of antimicrobial agents
ST heterocyclic furanoflavonoid analog antifungal prepn
IT Fungicides
(synthesis of 4-hydroxy-1-methylindole and benzo[b]thiophen-4-ol based unnatural flavonoids as new class of antifungal agents)
IT Flavonoids
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of 4-hydroxy-1-methylindole and benzo[b]thiophen-4-ol based unnatural flavonoids as new class of antifungal a

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55 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN

CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 22, 27

TI Intramolecular cycloadditions with isobenzofurans. XI. Synthesis of annulated indoles

ST intramol cycloaddn isobenzofuran; annulated indole prepn; furoindole prepn; furo indole formation intramol Diels Alder; quantum chem calcn cycloaddn furoindole benzofuran

IT Quantum chemistry
(PM3; of cycloaddn. of furoindole and benzofuran)

IT Density-functional theory
Potential energy surface and hypersurface
(of cycloaddn. of furoindole and benzofuran)

IT Molecular orbital
(AM1, of cycloaddn. of furoindole and benzofuran)

IT Cycloaddition reaction
Diels-Alder reaction
(intramol., of furoindole and benzofuran)

IT 35185-96-7 182205-37-4

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55 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
IC ICM A61K031-40
ICS A61K031-44; C07D491-052; C07D491-00
INCL 514411000
CC 1-11 (Pharmacology)
Section cross-reference(s): 28
TI 2-(Aminomethyl)-3,4,7,9-tetrahydro-2h-pyrano-[2,3-e]indol-8-ones and derivatives
ST aminomethyltetrahydropyranoindol prepn dopamine agonist; nervous system agent aminomethyltetrahydropyranoindol; autoreceptor dopamine agonist aminomethyltetrahydropyranoindol
IT Drug delivery systems
Nervous system agents
Schizophrenia

10514427

55 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
IC ICM A61K031-541
ICS A61K031-5377; A61K031-496; A61K031-454; A61K031-407; C07D491-02; C07D498-02
INCL 514217090; 514227800; 514232500; 514254080; 514320000; 514411000; 540602000; 544060000; 544142000; 544372000
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
TI Preparation of 3-[(hetero)arylsulfonyl]-tetrahydro-3H-benzo[e]indol-8-amines as 5-hydroxytryptamine-6 ligands
ST heteroarylsulfonyltetrahydrobenzoindolamine prepn hydroxytryptamine 5HT6 ligand; serotonin 5HT6 ligand benzoindolamine heteroarylsulfonyl prepn
IT Mental and behavioral disorders
(attention deficit disorder; preparation of 3-[(hetero)arylsulfonyl]-tetrahydro-3H-benzo[e]indol-8-amines as 5-hydroxytryptamine-6 ligands for treating CNS disorders)
IT Nervous system, disease